

## ORIGINAL RESEARCH

# Anthropometry-based prediction of body composition in early infancy compared to air-displacement plethysmography

Laurentya Olga<sup>1</sup>  | Inge A. L. P. van Beijsterveldt<sup>2</sup>  | Ieuan A. Hughes<sup>1</sup> |  
David B. Dunger<sup>1,3</sup> | Ken K. Ong<sup>1,3,4</sup> | Anita C. S. Hokken-Koelega<sup>2</sup> |  
Emanuella De Lucia Rolfe<sup>4</sup>

<sup>1</sup>Department of Paediatrics, University of Cambridge, Cambridge, UK

<sup>2</sup>Department of Pediatrics, Subdivision of Endocrinology, Erasmus University Medical Center-Sophia Children's Hospital, Rotterdam, The Netherlands

<sup>3</sup>Institute of Metabolic Science, University of Cambridge, Cambridge, UK

<sup>4</sup>MRC Epidemiology Unit, University of Cambridge, Cambridge, UK

## Correspondence

Emanuella De Lucia Rolfe, MRC Epidemiology Unit, University of Cambridge, School of Clinical Medicine, Box 285; Institute of Metabolic Science, Cambridge Biomedical Campus, Cambridge CB2 0QQ, United Kingdom.  
Email: emanuella.de-lucia-rolfe@mrc-epid.cam.ac.uk

## Funding information

Biotechnology and Biological Sciences Research Council, Grant/Award Number: BB/P028195/1; Danone Nutricia Research; EU Commission for JPI HDHL program 'Call III Biomarkers' for project: BioFN - Biomarkers for Infant Fat Mass Development and Nutrition, Grant/Award Number: 696295; Medical Research Council Epidemiology Unit, Grant/Award Numbers: MC\_UU\_00006/2, MC\_UU\_12015/2; NIHR Cambridge Biomedical Research, Grant/Award Number: IS-BRC-1215-20014; ZonMw, Grant/Award Number: 529051013

## Summary

**Background:** Anthropometry-based equations are commonly used to estimate infant body composition. However, existing equations were designed for newborns or adolescents. We aimed to (a) derive new prediction equations in infancy against air-displacement plethysmography (ADP-PEA Pod) as the criterion, (b) validate the newly developed equations in an independent infant cohort and (c) compare them with published equations (Slaughter-1988, Aris-2013, Catalano-1995).

**Methods:** Cambridge Baby Growth Study (CBGS), UK, had anthropometry data at 6 weeks (N = 55) and 3 months (N = 64), including skinfold thicknesses (SFT) at four sites (triceps, subscapular, quadriceps and flank) and ADP-derived total body fat mass (FM) and fat-free mass (FFM). Prediction equations for FM and FFM were developed in CBGS using linear regression models and were validated in Sophia Pluto cohort, the Netherlands, (N = 571 and N = 447 aged 3 and 6 months, respectively) using Bland-Altman analyses to assess bias and 95% limits of agreement (LOA).

**Results:** CBGS equations consisted of sex, age, weight, length and SFT from three sites and explained 65% of the variance in FM and 79% in FFM. In Sophia Pluto, these equations showed smaller mean bias than the three published equations in estimating FM: mean bias (LOA) 0.008 (−0.489, 0.505) kg at 3 months and 0.084 (−0.545, 0.713) kg at 6 months. Mean bias in estimating FFM was 0.099 (−0.394, 0.592) kg at 3 months and −0.021 (−0.663, 0.621) kg at 6 months.

**Conclusions:** CBGS prediction equations for infant FM and FFM showed better validity in an independent cohort at ages 3 and 6 months than existing equations.

## 1 | INTRODUCTION

Nutritional and growth patterns during early life have been associated with risks for obesity and cardiometabolic diseases later in life.<sup>1–4</sup> This association has been continuously reported even in the current

Laurentya Olga and Inge A. L. P. van Beijsterveldt should be considered joint first author. Emanuella De Lucia Rolfe and Anita C. S. Hokken-Koelega should be considered joint senior author.

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studies and reviews.<sup>5-7</sup> Quantification of infant body composition enables accurate estimation of the effects of early-life nutrition on growth and the putative developmental mechanisms leading to later co-morbidities. Weight for length and body mass index (BMI) are widely used as early adiposity screening tools<sup>8</sup>; however, those parameters do not distinguish between fat mass (FM) and fat-free mass (FFM), the relative proportions of which vary markedly during infancy.<sup>9</sup> Moreover, in pediatric population, BMI often produces imprecise estimate of adiposity, and it varies greatly with age and gender.<sup>10,11</sup>

Several methods are available to assess infant body composition. These include dual-energy X-ray absorptiometry (DXA),<sup>12</sup> quantitative nuclear magnetic resonance (QMR),<sup>13</sup> bioelectrical impedance analysis (BIA),<sup>14</sup> total body electrical conductivity (TOBEC),<sup>15</sup> stable isotope dilution and air-displacement plethysmography (ADP). BIA and TOBEC are non-invasive, safe, portable, inexpensive and widely available, but their use in infants is limited by poor accuracy.<sup>14-18</sup> Prediction studies in infants using BIA as the criterion are also scarce.<sup>17,18</sup> DXA and QMR provide more accurate estimates of infant body composition; however, they are often infeasible because they require infants to lie still, even with the use of sedative agents.<sup>12,13</sup> In addition, DXA uses ionizing radiation, and results could vary depending on the type of scans and softwares used.<sup>19-22</sup> Accordingly, the use of DXA in infants is limited, and detailed body composition data in this population are not abundant.<sup>17,18</sup>

ADP-PEA Pod is a non-invasive whole-body densitometry device to estimate infant body composition (total body FM and FFM). It is accurate and reliable in young infants when assessed against DXA,<sup>23-25</sup> although there was also a study reporting high correlation between those two instruments with significant difference.<sup>19</sup> Nevertheless, ADP-PEA Pod is limited to infants weighing between 1 and 8 kg, thus usually it cannot be used for infants older than 6 months. The equipment is relatively expensive, is not portable, and the process is often time-consuming, so is impractical to use in many large-scale population studies.<sup>26</sup> Furthermore, some parents report anxiety in leaving their young infants in the closed ADP-PEA Pod system for around 2 minutes.<sup>26</sup> Therefore, in research studies, estimates of infant body composition are often derived using anthropometry-based

equations.<sup>8,27</sup> However, many of those equations include uncommonly collected measures (eg, calf circumference<sup>28</sup> and flank skinfolds<sup>29</sup>) that are not available in infant cohort studies.

In this study, we aimed to develop new anthropometry-based equations for the prediction of total body FM and FFM in infancy against ADP-PEA Pod as the criterion, in a UK cohort, the Cambridge Baby Growth Study (CBGS). We also aimed to determine the accuracy of these new equations and three existing childhood anthropometry-based equations (Slaughter et al,<sup>16</sup> Aris et al<sup>23</sup> and Catalano et al,<sup>30</sup> Table 1), in an independent birth cohort, Sophia Pluto study, the Netherlands, using ADP-PEA Pod as the reference method. While Aris et al<sup>23</sup> and Catalano et al<sup>30</sup> were derived among neonatal populations, Slaughter et al<sup>16</sup> involved individuals aged 8-29 years old. Although the age range used in those three published equations was different from ours, they are frequently used in studies involving infants and children and were built using relevant anthropometry measures and skinfold sites.

## 2 | SUBJECTS AND METHODS

### 2.1 | Derivation cohort

The new anthropometry-based prediction equations were derived in CBGS, a longitudinal birth cohort study set up in 2001 at a single maternity hospital in Cambridge, United Kingdom, to investigate the prenatal and postnatal determinants of infancy weight gain, body composition and adiposity.<sup>31</sup> To provide detailed growth measures in the first weeks of life, N = 150 mother-infant pairs born between 2015 and 2018 underwent a more intensive measurement protocol. All infants were singleton, vaginally delivered at term, of normal weight mothers with no significant pregnancy comorbidities and had normal birth weight. This analysis included a cohort subgroup of 77 infants with ADP-PEA Pod measurements. There were in total 119 measurements employed to derive the equations, N = 55 at 6 weeks and N = 64 at 3 months. There was no significant difference in 6 weeks and 3 months anthropometry between the subgroup and the whole cohort (data not shown). The study was approved by the Cambridge Local Research Ethics Committee, and all mothers gave written informed consent.

**TABLE 1** Published anthropometry-based prediction equations for body composition in children

First author (year)	Prediction equation	SFT site(s)	Participants age	Reference method
Slaughter et al (1988) <sup>16</sup>	Boys: % BF = 1.21 x Sum SFT – 0.008 x (Sum SF) <sup>2</sup> – 1.7 Girls: % BF = 1.33 x Sum SFT – 0.013 x (Sum SF) <sup>2</sup> – 2.5	Triceps and Subscapular (mm)	8–29 years old	Underwater weighing to measure body density and deuterium oxide dilution to measure body water
Aris et al (2013) <sup>23</sup>	FM (kg) = –0.022 + 0.307 * Weight (kg) – 0.077 x Sex (1 = boy; 0 = girl) – 0.019 x GA (weeks) + 0.028 x SFT	Subscapular (mm)	1–3 days old	ADP-PEA Pod
Catalano et al (1995) <sup>30</sup>	FM (kg) = 0.54657 + 0.39055 x Weight (kg) + 0.0453 x SFT – 0.03237 x Length (cm)	Flank (mm)	1–3 days old	TOBEC

Abbreviations: FM, fat mass; FFM, fat-free mass; GA, gestational age; SFT, skinfold thickness; TOBEC, total body electrical conductivity.

## 2.2 | Validation cohort

The anthropometry-based equations developed in CBGS were validated in an independent birth cohort study, Sophia Pluto, a prospective study to collect longitudinal data on measured growth and body composition among large group of healthy infants born at term. Mothers were recruited between 2013 and 2018, from several maternity wards in and near Rotterdam, the Netherlands.

## 2.3 | Infant anthropometry

Infant anthropometry data were collected by trained pediatric research nurses, following standard protocols. Weight was measured to the nearest 1 g using a Seca 757 electronic baby scale (Seca, Birmingham, UK). Length was measured to the nearest 0.1 cm using an Infantometer (Seca 416). Waist circumference was measured at the midpoint between the lowest rib margin and the iliac crest to the nearest 0.1 cm using a non-stretchable fiber-glass tape (Chasmors Ltd, London, United Kingdom) in CBGS and a measuring tape (Seca, Hamburg, Germany) in Sophia Pluto. Skinfold thickness (SFT) measures were taken in triplicate from the left side of the body at four sites, including triceps, subscapular, flank (suprailiac), biceps (Sophia Pluto only) and quadriceps (CBGS only) using a calibrated Holtain Tanner/Whitehouse Skinfold Caliper (Holtain, Crymych, United Kingdom) in CBGS and using a Skinfold caliper (Slimguide C-120, Creative Health) in Sophia Pluto. Infant body composition parameters (% body fat, FM and FFM) were estimated using ADP-

PEA Pod (COSMED/Life Measurement Inc., Concord, California), which directly measures body volume and body weight to calculate body density. Infant % body fat was calculated from body density assuming the density of fat to be 0.9007 kg/L. Age- and gender-specific densities of FFM were computed using the data of Fomon et al.<sup>32</sup> FM and FFM were calculated from body weight and % body fat. ADP-PEA Pod was calibrated every day, according to the instructions of the manufacturer. In the CBGS, ADP-PEA Pod was conducted twice, at 6 weeks and 3 months old, while in Sophia Pluto, it was conducted twice at 3 and 6 months.

## 2.4 | Statistical analysis

In CBGS, stepwise multivariable regression models were performed to derive the optimal prediction of ADP-PEA Pod derived FM and FFM, using sex, age, length, weight and skinfold thicknesses as independent variables. The equations involved three sites of skinfolds measurement which were commonly measured by both studies: triceps, subscapular and flank (suprailiac). Quadriceps skinfold was omitted due to its unavailability in the validation cohort.

In Sophia Pluto, FM and FFM values were predicted using newly developed equations and three other childhood prediction equations (Table 1). Agreement between predicted and ADP-PEA Pod measured FM and FFM values was assessed using one-sample paired Student's *t* test, bivariate correlation, linear regression analysis and Bland-Altman analyses. In each Bland-Altman plot, the y-axis represents the difference or bias between equation-predicted and ADP-

**TABLE 2** Baseline cohorts' characteristics by sex

Descriptive	Cohort				P value <sup>*</sup>	
	CBGS (N = 77)		Sophia Pluto (N = 571)			
	Boys (55%)	Girls (45%)	Boys (54%)	Girls (46%)	Boys	Girls
Birth						
GA (weeks)	40.05 ± 1.17	40.13 ± 1.15	39.65 ± 1.24	39.77 ± 1.24	0.048	0.008
Weight (kg)	3.55 ± 0.47	3.47 ± 0.4	3.45 ± 0.49 <sup>b</sup>	3.31 ± 0.5	0.211	0.072
Length (cm) <sup>a</sup>	50.79 ± 1.89	50.21 ± 1.55	50.84 ± 2.18	49.91 ± 2.04	0.889	0.412
3 months						
Weight (kg)	6.29 ± 0.73 <sup>b</sup>	5.65 ± 0.54	6.26 ± 0.70 <sup>b</sup>	5.70 ± 0.69	0.795	0.682
Length (cm)	60.87 ± 2.12 <sup>b</sup>	59.58 ± 1.74	61.95 ± 2.07 <sup>b</sup>	60.23 ± 2.18	<0.010	0.089
FM (kg)	1.42 ± 0.37	1.29 ± 0.39	1.42 ± 0.41 <sup>b</sup>	1.32 ± 0.4	1.000	0.675
FFM (kg)	4.78 ± 0.42 <sup>b</sup>	4.42 ± 0.47	4.84 ± 0.47 <sup>b</sup>	4.37 ± 0.42	0.430	0.516
FMI (kg/m <sup>2</sup> )	3.85 ± 0.98	3.62 ± 1.04	3.68 ± 1.01	3.62 ± 1.02	0.313	0.96
FFMI (kg/m <sup>2</sup> )	12.95 ± 0.88 <sup>b</sup>	12.41 ± 0.95	12.57 ± 0.91 <sup>b</sup>	12.05 ± 0.86	0.011	0.022

Note: Values are mean ± SD. FMI, fat mass index, calculated by dividing FM (kg) by length squared (m<sup>2</sup>).<sup>26</sup> FFMI, fat-free mass index, calculated by dividing FFM (kg) by length squared (m<sup>2</sup>).<sup>26</sup> P values are based on independent *t* test.

Abbreviations: GA, gestational age; FFM, fat-free mass; FM, fat mass.

Significant *p*-values (< 0.05) are indicated in bold.

<sup>\*</sup>P value between CBGS and Sophia Pluto of the same genders (ie, boys = CBGS boys vs Sophia Pluto boys, girls = CBGS girls vs Sophia Pluto girls).

<sup>a</sup>Birth length available in Sophia Pluto cohort: boys *n* = 210, girls *n* = 152.

<sup>b</sup>Significantly different between boys and girls (*P* < .005) in the same infant group (ie, CBGS boys vs girls, Sophia Pluto boys vs girls).

PEA Pod measured values with limits of agreement (LOA) described as the 95% confidence range (mean bias  $\pm$  1.96 SDs), while the x-axis represents the mean values of the two methods being compared (FM or FFM predicted from each corresponding equation and their absolute measured values from ADP-PEA Pod). The possibility of predicted results being affected by the magnitude of the measured values was assessed by running a correlation analysis between the mean (of the values measured by ADP-PEA Pod as the reference and each alternative equation) and the difference of values between the reference and each equation. Moreover, proportional bias was also calculated using linear regression, with the difference between measured and predicted FM/FFM acting as the dependent variable while the average of measured and predicted FM/FFM acting as the independent variable.

Statistical analyses were performed using SPSS version 25.0 (IBM) and R version 1.0.136. A *P* value less than .05 was considered statistically significant.

### 3 | RESULTS

Baseline characteristics of derivation and validation cohorts are summarized in Table 2. At birth, CBGS infants were heavier than Sophia Pluto's with comparable length. In contrast, both cohorts had similar weight average, while CBGS infants were shorter at 3 months of age. In addition, 92.4% CBGS subjects were of Caucasian, while Sophia Pluto included a more diverse population with 62.6% Caucasian (of which 93.8% were white Caucasian and 6.2% were Turkish/

**TABLE 3** CBGS-derived equations to predict ADP-PEA Pod measured infant FM and FFM combining 6 weeks and 3 months measurements

Model		wt (Kg)	L (cm)	Sex	Age (days)	SFT-t (mm)	SFT-s (mm)	SFT-f (mm)	Constant	R <sup>2</sup>	RMSE
<b>Dependent variable: FM (kg)</b>											
1	Wt + L + Sex + Age	B $\pm$ SE	0.624 $\pm$ 0.06*	-0.088 $\pm$ 0.02*	-0.07 $\pm$ 0.05	0.001 $\pm$ 0.002			2.87 $\pm$ 0.79	0.63	0.262
2	Model 1 + SFT	B $\pm$ SE	0.512 $\pm$ 0.08*	-0.074 $\pm$ 0.02*	-0.037 $\pm$ 0.05	0.002 $\pm$ 0.002	0.041 $\pm$ 0.02	0.008 $\pm$ 0.03	0.011 $\pm$ 0.02	2.167 $\pm$ 0.86	0.65 0.258
<b>Dependent variable: FFM (kg)</b>											
1	Wt + L + Sex + Age	B $\pm$ SE	0.407 $\pm$ 0.06*	0.067 $\pm$ 0.02*	0.034 $\pm$ 0.05	-0.002 $\pm$ 0.002			-1.703 $\pm$ 0.83	0.77	0.276
2	Model 1 + SFT	B $\pm$ SE	0.528 $\pm$ 0.08*	0.052 $\pm$ 0.02*	-0.001 $\pm$ 0.06	-0.002 $\pm$ 0.002	-0.005 $\pm$ 0.03	-0.014 $\pm$ 0.02	-0.046 $\pm$ 0.02*	-0.954 $\pm$ 0.9	0.79 0.271

Note: Based on 119 infant measurements at ages 5-16 weeks.

Abbreviations: B, unstandardized beta; FFM, fat-free mass; FM, fat mass; L, length (cm); RMSE, root mean squared error; SE, standard error; sex, (1 = male, 0 = female); SFT-f, flank (suprailiac); SFT-s, subscapular; SFT-t, triceps Skinfold thickness; wt, weight.

\**p* < 0.05 for statistically significant B.

**TABLE 4** FM and FFM values predicted by anthropometry-based equations vs measured by ADP-PEA Pod among Sophia Pluto infants

	Slaughter et al	Aris et al	Catalano et al	CBGS (no SFT)	CBGS (with SFT)	ADP-PEA Pod
<b>Age 3 months</b>						
N = 571 (264 girls), mean age = 92.3 days						
FM (kg)	Boys: 1.00 $\pm$ 0.27 Girls: 0.88 $\pm$ 0.23	1.23 $\pm$ 0.24	1.25 $\pm$ 0.30	1.29 $\pm$ 0.34	1.39 $\pm$ 0.35 <sup>a</sup>	All: 1.37 $\pm$ 0.41 Boys: 1.42 $\pm$ 0.41 Girls: 1.32 $\pm$ 0.4
FFM (kg)	NA	NA	NA	4.68 $\pm$ 0.43	4.74 $\pm$ 0.45	All: 4.62 $\pm$ 0.5 Boys: 4.84 $\pm$ 0.47 Girls: 4.37 $\pm$ 0.42
<b>Age 6 months</b>						
N = 447 (211 girls), mean age = 183.4 days						
FM (kg)	Boys: 1.28 $\pm$ 0.32 Girls: 1.18 $\pm$ 0.31	1.73 $\pm$ 0.29	1.69 $\pm$ 0.36	1.84 $\pm$ 0.43	1.96 $\pm$ 0.42	All: 1.86 $\pm$ 0.51 Boys: 1.85 $\pm$ 0.51 Girls: 1.86 $\pm$ 0.51
FFM (kg)	NA	NA	NA	5.62 $\pm$ 0.49	5.77 $\pm$ 0.52 <sup>b</sup>	All: 5.76 $\pm$ 0.58 Boys: 6.02 $\pm$ 0.53 Girls: 5.46 $\pm$ 0.49

Note: Values are mean  $\pm$  SD. Paired *t* test (compared to ADP-PEA Pod), all *P* < .05, except <sup>a</sup>*P* = .402 and <sup>b</sup>*P* = .171.

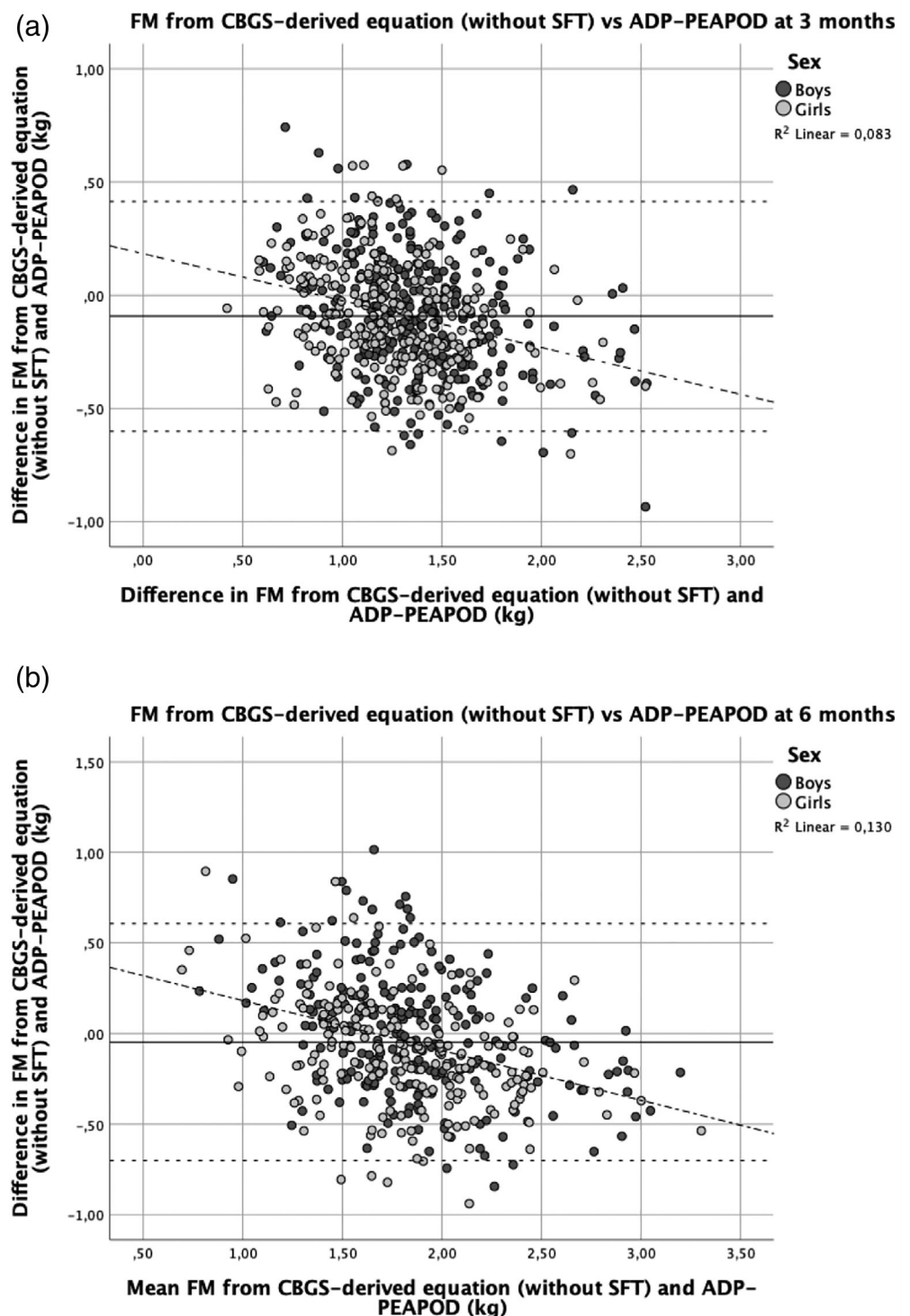
Abbreviations: FFM, fat-free mass; FM, fat-mass; NA, not applicable.

Moroccan), 27.1% of mixed ethnicities and the remaining 10.3% of other ethnicities (Asian, African, Latin American).

### 3.1 | Derivation of anthropometry-based prediction equations

Infant weight and length appeared as significant predictors of infant body composition, while infant sex, gestational age (GA) and postnatal age at

visit were not. However, since the equations were derived using the stepwise method with pragmatic approach, infant sex and age at visit were still included in the models. The proportion of variance explained by the derived prediction equations was greater in FFM than FM models. Infant weight, length, sex and visit age explained 63% and 77% variance of the FM and FFM models, respectively (Table 3). The addition of SFTs only added a further 2% of variance proportion explained in both FM and FFM models. Furthermore, among the three SFT sites included, only flank SFT appeared as a significant predictor of infant FFM.



**FIGURE 1** Bland-Altman plots showing mean bias (solid line) and limits of agreement (LOA, represented by 95% CI; dotted horizontal line) between FM values estimated by the CBGS equation (without skinfolds) vs values measured by ADP-PEA Pod as the criterion method among Sophia Pluto infants at age 3 A, and 6 months B,

We also developed a number of other prediction equations for FM and FFM in CBGS using subsets of the available infant anthropometry parameters. While their predictive abilities are somewhat weaker than the above equations, these will allow a wider application in infant cohort studies that have collected limited anthropometric measurements (Table S1). The final equations to be validated in the Sophia Pluto (Table 3) were chosen by taking  $R^2$  and root mean squared error (RMSE) into consideration.

### 3.2 | Independent validation in Sophia Pluto

The performance of CBGS equations was assessed against ADP-PEA Pod-measured FM values as the criterion in Sophia Pluto infants and compared to three existing childhood equations. The CBGS equation was the only method that had the least significant difference (Table 4). Predicted values from CBGS equations did not differ with the absolute values from ADP-PEA Pod for FM at

3 months ( $P = .402$ ) and for FFM at 6 months ( $P = .171$ ). Accordingly, while all five equations predicted FM with strong positive correlations with ADP-PEA Pod measured FM values at both 3 and 6 months (Pearson coefficients  $>0.7$ ), mean bias was lowest for CBGS-derived FM values (0.008 kg; LOA  $-0.489, 0.505$ ) (Figure 1 and Table 5). All of the correlation analyses between the mean (of the values measured by ADP-PEA Pod as the reference and each alternative equation) and the difference of values between the reference and each equation resulted in significant negative correlations, with CBGS equations had the least negative Pearson correlation coefficients (Table 5). Negative proportional bias was also detected for predicted FM values derived from all four equations, but again the extent of this bias was smallest when using the CBGS equations (Table 5 and Figure S1).

FFM was predicted only using CBGS equations, and these values were strongly correlated with FFM measured by ADP-PEA Pod at both time points (Pearson coefficients  $>0.8$ ). Similarly, FFM predicted by CBGS equations showed small mean bias compared to ADP-PEA Pod measured FFM (0.099 kg; LOA:  $-0.394, 0.592$ ).

**TABLE 5** Bland and Altman and regression analyses of body composition values estimated by prediction equations against ADP-PEA Pod measurements

	Correlation		Bland-Altman		Proportional Bias		Correlation between mean and difference <sup>a</sup>	
	Pearson R	P	Mean Bias	LOA (95% CI)	B $\pm$ SE	P	Pearson R	P
<b>Age 3 months</b>								
<b>FM</b>								
Slaughter et al (boys)	0.736	<.001	-0.422	-0.987, 0.143	-0.470 $\pm$ 0.043	<.001	-0.535	<.001
Slaughter et al (girls)	0.730	<.001	-0.440	-1.000, 0.123	-0.613 $\pm$ 0.045	<.001	-0.645	<.001
Aris et al	0.798	<.001	-0.151	-0.675, 0.373	-0.570 $\pm$ 0.026	<.001	-0.676	<.001
Catalano et al	0.800	<.001	-0.131	-0.628, 0.366	-0.348 $\pm$ 0.027	<.001	-0.472	<.001
CBGS-no SFT	0.785	<.001	-0.093	-0.6, 0.414	-0.207 $\pm$ 0.029	<.001	-0.288	<.001
CBGS-with SFT	0.794	<.001	0.008	-0.489, 0.505	-0.189 $\pm$ 0.028	<.001	-0.271	<.001
<b>FFM</b>								
CBGS-no SFT	0.867	<.001	0.049	-0.453, 0.551	-0.178 $\pm$ 0.022	<.001	-0.318	<.001
CBGS-with SFT	0.872	<.001	0.099	-0.394, 0.592	-0.125 $\pm$ 0.022	<.001	-0.234	<.001
<b>Age 6 months</b>								
<b>FM</b>								
Slaughter et al (boys)	0.722	<.001	-0.589	-1.317, 0.139	-0.600 $\pm$ 0.049	<.001	-0.630	<.001
Slaughter et al (girls)	0.733	<.001	-0.677	-1.382, 0.029	-0.592 $\pm$ 0.050	<.001	-0.637	<.001
Aris et al	0.755	<.001	-0.144	-0.860, 0.572	-0.718 $\pm$ 0.032	<.001	-0.736	<.001
Catalano et al	0.774	<.001	-0.192	-0.852, 0.468	-0.469 $\pm$ 0.032	<.001	-0.568	<.001
CBGS-no SFT	0.767	<.001	-0.048	-0.702, 0.606	-0.275 $\pm$ 0.034	<.001	-0.361	<.001
CBGS-with SFT	0.789	<.001	0.084	-0.545, 0.713	-0.300 $\pm$ 0.032	<.001	-0.410	<.001
<b>FFM</b>								
CBGS-no SFT	0.821	<.001	-0.171	-0.833, 0.491	-0.261 $\pm$ 0.029	<.001	-0.390	<.001
CBGS-with SFT	0.832	<.001	-0.021	-0.663, 0.621	-0.188 $\pm$ 0.029	<.001	-0.299	<.001

Abbreviations: B, unstandardized beta; CI, confidence interval; FFM, fat-free mass; FM, fat mass; LOA, limit of agreement; SE, standard error of B; SFT, skinfold thicknesses.

<sup>a</sup>Correlation between the mean (of the reference/ADP-PEA Pod and each alternative equation) and the difference between methods.



## 4 | DISCUSSION

In this study, we derived new anthropometry-based prediction equations for FM and FFM in UK infants aged 5-16 weeks using ADP-PEA Pod as the criterion method. In the CBGS, infant weight and length appeared as significant predictors of infant body composition, whereas infant sex, gestational age (GA) and postnatal age at visit were not. Using stepwise method with pragmatic approach to derive the prediction equations, infant sex and age at visit were still included in the models. Many studies have reported that there are sex differences in body composition.<sup>33,34</sup> These equations were then validated among Dutch infants aged 3 and 6 months in an independent cohort, Sophia Pluto.

In the Sophia Pluto cohort, the CBGS-derived equations produced more accurate predictions of infant FM compared to the other existing FM prediction equations published by Slaughter et al, Aris et al and Catalano et al. Based on paired *t* test, predicted values from CBGS equations were the most accurate to ADP-PEA Pod results compared to the other published equations, in both FM and FFM.

Of note, although the participants involved in Slaughter's equations were much older than our infant population (Table 2), comparing our equation to theirs is still considered relevant. This is because Slaughter's equations are frequently used in studies involving pediatric population, including those of younger groups,<sup>12,23</sup> especially when data harmonization is needed across cohorts.<sup>35</sup>

All equations produced significant negative proportional biases (Table 5), suggesting negative correlations between the mean and the difference of the predicted vs the actual FM/FFM values. This means that the performance of each equation depends on the magnitude of the actual values of FM/FFM, and all equations tend to over- and underestimate FM/FFM in those with lower and higher measured values (by the ADP-PEA Pod), respectively. Compared to the other equations, CBGS equations had the smallest proportional biases.

To our knowledge, this is one of the few studies testing the combinations of anthropometric parameters to build body composition prediction equations with the use of ADP-PEA Pod as the criterion method. We aimed to predict absolute FM and FFM, rather than relative or % body fat, since previous studies have reported better correlations between those absolute values with anthropometry.<sup>33</sup> The correlation coefficients of predicted and measured values of FFM were slightly higher than FM values, but the mean differences were similar.

We observed that weight and length were the main contributors in predicting infant FM and FFM. Infant weight has been consistently reported in previous studies to be the most essential predictor of infant FM.<sup>23,27,33</sup> Apart from weight, Deierlein et al reported that other predictors included infant SFT (triceps, subscapular and quadriceps), sex, age at measurement and ethnicity.<sup>27</sup> Infant weight and sex were also described predictors of infant FM in a Singapore cohort (Aris et al), together with GA.<sup>23</sup> However, we did not find infant sex or GA to be significant contributors to our prediction equations. We postulate that this is due to the limited heterogeneity in ethnicity among CBGS infants, and the difference in age range covered by

CBGS (5-16 weeks) compared to those other studies (1-3 days post-delivery).<sup>23,36</sup> Nonetheless, although they were not statistically significant, we still included infant sex and age at measurement in the prediction equations as biologically plausible contributors.

We found that SFTs contributed only modestly to the prediction of both FM and FFM. Lingwood et al also found that SFT did not improve their predictions equations beyond weight, length and sex.<sup>33</sup> Nonetheless, SFT were still included in the equations (Table 3) since they increased the  $R^2$ , decreased the RMSE and therefore increased the precision of the equations, although not by much.

Furthermore, of all three SFT sites included in the equations, only flank SFT appeared to be a significant independent predictor of infant FFM (Table 3). Since flank skinfold reflects central adiposity, this result could be speculatively interpreted as central fatness contributing more to the FFM estimation. However, if all SFT sites in CBGS cohort were considered, additional analyses showed that both flank and quadriceps SFTs were the most significant contributors to the prediction of FFM (Supplementary materials). Interestingly, flank SFT was also determined as the most significant FM predictor in Catalano's equation.<sup>30</sup> Since Sophia Pluto did not measure quadriceps SFT, this parameter could not be included in the equations taken forward for validation.

The proportional biases in the CBGS equations were smaller than those of the other equations, but they were all significant when compared to the criteria method (ADP-PEA Pod, Table 5 and Figure S1). Therefore, accurate body composition measurement during infancy should be pursued by ADP-Pea Pod or DXA, whilst equations can be employed as proxies to estimate fat/fat-free mass where body composition instrument is not available.

While the derivation sample included a wide distribution of % body fat (6.5-38.6%) and a relatively wide age range (38-112 days), we acknowledge some limitations. Firstly, the skinfold thickness measurements in the derivation and validation cohorts were conducted using different tools. However, despite the use of different calipers, the CBGS equations still produced smaller proportional biases compared to the other established equations. Second, since all CBGS infants were vaginally delivered with normal birth weight and born of healthy mothers with normal pre-pregnancy BMI, the equations might not be applicable in population with a high rate of Caesarean section and high variance of maternal pre-pregnancy BMI or infant's birth weight. Third, both prediction and validation cohorts included only healthy and term infants, thus our findings may not relevant for preterm infants. However, our validation cohort also included severe small-for-gestational-age (SGA) infants with birthweight/length less than  $-2.5$  z-score. Regarding ethnicity, although our derivation cohort was predominantly white Europeans, Sophia Pluto as the independent validation cohort included more diverse ethnicities with at least 37% of them were non-Caucasian. Although Aris et al did not find ethnicity to be significant in their FM equation derived in Asian infants,<sup>23</sup> a recent systematic review reported differences in infant body composition between ethnicities.<sup>37</sup> Therefore, the applicability of our equations to other ethnic populations remains in question.

## 5 | CONCLUSIONS

We derived and validated new anthropometry-based equations for infant FM and FFM using simple parameters often measured in infant studies. These new equations appeared to be more robust in predicting infant FM and FFM when compared to other published childhood equations despite the presence of proportional bias. These equations are fit for use in longitudinal infant cohorts or trials, when reference methods, such as ADP-PEA Pod, are not feasible.

## ACKNOWLEDGEMENTS

### CBGS

The authors are grateful to the CBGS research nurses Suzanne Smith, Ann-Marie Wardell and Karen Forbes, Addenbrooke's Hospital, Cambridge. We thank all the families who contributed to the study, the staff at the NIHR-Wellcome Trust Clinical Research Facility, Cambridge the NIHR Cambridge Comprehensive Biomedical Research Centre and the midwives at the Rosie Maternity Hospital, Cambridge, UK.

### Sophia Pluto

The authors want to thank all parents for their participation in the Sophia Pluto study and greatly acknowledge the research nurses Janneke van Nieuwkesteele, Christel Bruinings-Vroombout, Marianne Huibregtse-Schouten, Esther Lems, Naomi Khieroe, Suzanne Besteman-Voortman, Jose Bontenbal-van de Wege.

## FUNDING

This work was supported by the EU Commission to the JPI HDHL program "Call III Biomarkers" for the project: BioFN—Biomarkers for Infant Fat Mass Development and Nutrition (Grant agreement No 696295), administrated in the Netherlands by the Netherlands Organisation for Health Research and Development (ZonMW) (grant number 529051013) and UK by the Biotechnology and Biological Sciences Research Council (BB/P028195/1). This study also supported by the National Institute for Health Research (NIHR) Cambridge Biomedical Research Centre (IS-BRC-1215-20014). K.K.O. is supported by Medical Research Council Epidemiology Unit (MC\_UU\_12015/2 and MC\_UU\_00006/2). The views expressed are those of the authors and not necessarily those of the funders.

The Sophia Pluto study is an investigator-initiated cohort study, for which A.C.S.H.K. received an independent research grant by Danone Nutricia Research.

All CBGS and Sophia Pluto study sponsors had no role in the study design, collection, analysis or interpretation of the data, the writing of the manuscript or the decision to submit it for publication.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## AUTHOR CONTRIBUTIONS

Laurentya Olga, Inge A. L. P. van Beijsterveldt, Emanuella De Lucia Rolfe and Anita C. S. Hokken-Koelega had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. David B. Dunger, Ken K. Ong and Ieuan A. Hughes were involved in the conduction of the CBGS and Anita C. S. Hokken-Koelega for Sophia Pluto. Laurentya Olga and Inge A. L. P. van Beijsterveldt were responsible for infant recruitment and clinic visit in the CBGS and Sophia Pluto, respectively. Laurentya Olga and Inge A. L. P. van Beijsterveldt performed statistical analyses. Laurentya Olga and Emanuella De Lucia Rolfe drafted the manuscript. Inge A. L. P. van Beijsterveldt, Anita C. S. Hokken-Koelega, Ken K. Ong, David B. Dunger and Ieuan A. Hughes helped to improve the manuscript. All authors contributed to interpretation of data, critically revised the article for important intellectual content and approved the final version.

## ORCID

Laurentya Olga  <https://orcid.org/0000-0002-3562-0598>

Inge A. L. P. van Beijsterveldt  <https://orcid.org/0000-0002-0204-7430>

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Olga L, van Beijsterveldt IALP, Hughes IA, et al. Anthropometry-based prediction of body composition in early infancy compared to air-displacement plethysmography. *Pediatric Obesity*. 2021;e12818. <https://doi.org/10.1111/ijpo.12818>